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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/425,075	10/21/1999	PRABHAKARA V. CHOUDARY	480.97-1-(HV)	9044

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EXAMINER

HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 04/16/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/425,075

Applicant(s)

CHOUDARY ET AL.

Examiner

Larry R. Helms

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 November 2002.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 36-50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 36-50 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

1. Claim 50 has been added.
2. Claims 36-50 are under examination.
3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

### *Response to Arguments*

4. The rejection of claims 36-40, 42-49 and newly added claim 50 under 35 U.S.C. 103(a) as being unpatentable over Horwitz et al (Proc. Natl. Acad. Sci. USA 85:8678-8682, 1988) and further in view of Cregg et al (Developments in Industrial Microbiology 29:33-41, 1988) and The Invitrogen 1997 Catalog (published 1/97, Yeast expression pages 14-17 and Master Catalog Amendment Notice for pPICZ vectors from 4/15/96) and Robinson et al (U.S. Patent 6,204,023, filed 6/6/95) is maintained.

The response filed 11/18/02 has been carefully considered but is deemed not to be persuasive. The response states that the Robinson reference leads one skilled in the art towards using single expression cassette vectors for expression in yeast in several places which is his preferred embodiment and leads one away from the use of dual expression cassette vectors and all working examples in yeast involve single expression cassettes and Robinson only discloses a dual cassette in expression in mammalian cells (see page 6-7 of response). In response to these arguments, while Robinson discloses a preferred embodiment, this does not teach away from the use of dual cassettes. In fact although Robinson uses a single expression cassette in yeast (see

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column 45-46) he also teaches that “in order for yeast to produce an intact functional antibody molecule a balanced synthesis of both light and heavy chain (underlined added) protein within the cell is preferred and one approach is to use separate vectors (see column 45, lines 50-55) , however, and also in light of Robinson’s teaching of “the inclusion of both heavy and light chain chimeric genes in the same plasmid allows for the introduction into transfected cells of a 1:1 gene ratio of the heavy and light chain genes leading to a balanced gene dosage” (underlined added) (see column 35, lines 59-64), one skill in the art would conclude that in order for a balanced synthesis the heavy and light chains can be on one plasmid in yeast.

The response further states that Robinson’s disclosure can not be extended to encompass *Pichia* (see pages 7-8 of response). In response to this argument, as evidenced from Lappi et al (U.S. Patent 5,916,772, filed 4/95) which was at the time of the claimed invention the term yeast clearly encompasses *S. cerevisiae* and *pichia pastoris* (see column 12, lines 10-15) and in view of the teachings of the invitrogen catalog which teaches *Pichia* for high levels of expression of protein it would have been obvious to use *Pichia* as the yeast strain.

The response further states that one of skill in the art would not practice the invention with any expectation of success and cites references as to the problems associated with intra-molecular recombination, transcriptional interference, translational interference (see pages 8-9 of response). In response to these arguments, the majority of the references are not concerned with antibodies and/or yeast cells and most are concerned with expression in *E.coli*. As taught by Horwitz et al antibodies can be

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expressed in yeast therefore one would have an expectation of success and in view of Robinson et al who teaches a single expression vector for the expression of the heavy and light chains in yeast, one would have an expectation of success to produce the antibody in Pichia with a single expression cassette.

In view of the teaching of Horwitz for production of an antibody in yeast and in view of the teaching of Robinson et al that a single expression cassette can be used for antibody production and the invitrogen catalog which describes vectors for expression in Pishia at high levels and Cregg et al for teaching a yeast promoter, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

5. The rejection of claims 36-49 and newly added claim 50 under 35 U.S.C. 103(a) as being unpatentable over Horwitz et al (PNAS 85:8678-8682, 1988) and further in view of Cregg et al (Developments in Industrial Microbiology 29:33-41, 1988) and The Invitrogen 1997 Catalog (published 1/97, Yeast expression pages 14-19 and Master Catalog Amendment Notice for pPICZ vectors from 4/15/96), Robinson et al (U.S. Patent 6,204,023, filed 6/6/95) and Vanderlaan et al (U.S. Patent 5,429,925, issued 7/4/95) is maintained.

The response filed 11/18/02 has been carefully considered but is deemed not to be persuasive. The response combined the arguments for both this rejection and the one above and added that Vanderlaan does nothing to cure the basic element lacking in the 103 rejection (see page 8 of response). In response to this argument, the response

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cited above is restated and in view of Vanderlaan one would produce an anti-digoxin antibody in view of the teachings of Horwitz et al, Cregg et al, The Invitrogen 1997 Catalog and Robinson et al as stated above.

### ***Conclusion***

6. No claim is allowed.
7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D., whose telephone number is

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(703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

A handwritten signature in black ink, appearing to be 'L. Helms', written in a cursive style.